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## Cytomegalovirus-Induced Thrombocytopenia in an Immunocompetent Adult

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THROMBOCYTOPENIA is an infrequent yet well-recognized complication of viral infection. Mumps, rubella, varicella, and infectious mononucleosis have each been documented to cause thrombocytopenia.<sup>1</sup> But although thrombocytopenia has been commonly observed in patients with congenital cytomegalovirus (CMV) infection,<sup>2</sup> it has rarely been reported after CMV infection in immunocompetent adults. We describe a case of profound thrombocytopenia that occurred ten weeks after a primary CMV infection.

### Report of a Case

The patient, a 31-year-old man, was seen because of sore throat for five days that was followed by a week of malaise, headache, loss of appetite, night sweats, and fever. He had no history of illnesses that would cause an immunodeficient state, and he had no risk factors for infection with the human immunodeficiency virus. The patient was previously in good health, was not receiving any medications, and had no history of transfusions or drug or alcohol abuse. On physical examination he had a temperature of 38.5°C (101.3°F) and a spleen palpable 1 cm below the costal margin. Laboratory tests revealed a leukocyte count of  $5.2 \times 10^9$  per liter (5,220 per  $\mu$ l), with 0.57 neutrophils, 0.24 lymphocytes (including many atypical forms), 0.08 bands, 0.06 monocytes, 0.04 eosinophils, and 0.01 basophils. The hemoglobin level was 145 grams per liter (14.5 grams per dl), and the platelet count was  $137 \times 10^9$  per liter (137,000 per  $\mu$ l). A prothrombin time, partial thromboplastin time, and erythrocyte sedimentation rate were normal. Blood chemistry

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TABLE 1.—Cases of Thrombocytopenia After Cytomegalovirus (CMV) Infection in Immunocompetent Adults

Source	Age, yr	Sex	Presentation	Interval	Platelet Count, $\times 10^9$ /liter	Diagnostic Tests	Treatment and Results
Chanarin and Walford, 1973 <sup>5</sup>	33	M	General purpura and gingival bleeding	3 wk after onset of illness	5	Titers 1:1,024 to 1:4,096; CMV cultured in urine	Prednisone, 60 mg/day for 3 wk and then tapered; platelet count, $139 \times 10^9$ /liter by day 16
Fiala and Kattlove, 1973 <sup>6</sup>	18	M	Confluent purpura, gingival bleeding, and petechiae	Several weeks after onset of infection	2	Positive IgM test; CMV cultured in buffy coat and urine	Prednisone, 120 mg/day for 16 days, then vincristine sulfate, 2 mg, followed by splenectomy on day 25; no response; prednisone therapy restarted; normal platelet count by day 46
Harris et al, 1975 <sup>7</sup>	27	M	Ecchymoses and petechiae	Beginning day 6 of illness	18	Titers 1:16 to 1:1,024; positive IgM test	Prednisone, 60 to 100 mg/day for 2 wk; little response; steroids tapered as CMV titers declined; platelet counts normal by 1 mo
Sahud and Bachelor, 1978 <sup>8</sup>	21	M	Shoulder pain, petechiae, and buccal hemorrhages	No preceding illness	12	Titers 1:1,024 to 1:16 after 3 mo	Refractory to high-dose steroids (persistent thrombocytopenia at 7 mo); bone marrow examination findings consistent with ITP; splenectomy, normal platelet count after several days
Shimm et al, 1980 <sup>9</sup>	20	M	Petechiae, gingival bleeding, and prolonged bleeding with shaving Fever, scattered petechiae	No preceding illness 4 wk after splenectomy	<10 38	Diagnosed as ITP by bone marrow examination CMV cultured in blood	Refractory to high-dose steroids; splenectomy at 7 wk; platelet count returned to normal Normal platelet count in 1 wk without treatment

IgM = immunoglobulin M, ITP = idiopathic thrombocytopenic purpura

# ABBREVIATIONS USED IN TEXT

CMV = cytomegalovirus  
Ig = immunoglobulin

values were also normal, with the exception of the lactate dehydrogenase (334 U per liter, normal 100 to 260), aspartate aminotransferase (70 U per liter, normal 7 to 40), and alanine aminotransferase (85 U per liter, normal 6 to 45). A chest roentgenogram was unremarkable, and both blood and urine cultures were sterile. Paul-Bunnell and Weil-Felix tests were negative, as was serologic testing for *Brucella* species, Q fever, the Epstein-Barr virus, *Salmonella typhi*, and *Haemophilus parainfluenzae*. An immunoglobulin (Ig) M titer was strongly positive for CMV, and there was a fourfold increase in IgG titers over two weeks (from < 1:20 to 1:80); CMV was later identified in the urine.

Four weeks after the symptoms started, the patient felt well. A hemogram and blood chemistry values were normal. After ten weeks, he noted easy bruisability and rectal bleeding. On examination he had ecchymoses over the lower extremities and scattered petechiae over the upper back. The platelet count was  $13 \times 10^9$  per liter, the hemoglobin was 151 grams per liter, and the leukocyte count was  $7.8 \times 10^9$  per liter. A regimen of prednisone, 40 mg per day, and aminocaproic acid, 3 grams per day, was begun. There was a modest increase in the number of platelets at one week, and aminocaproic acid was discontinued shortly thereafter. At the end of three weeks, the platelet count was only  $36 \times 10^9$  per liter. The prednisone dosage was doubled to 80 mg per day for two weeks and was subsequently tapered after the platelet count reached  $52 \times 10^9$  per liter. The prednisone therapy was discontinued after 11 weeks, and the platelet count stabilized at  $113 \times 10^9$  per liter after four months.

After three years of follow-up, the patient continues to be in good health. Platelet counts have always been higher than  $100 \times 10^9$  per liter.

## Discussion

Infection with CMV is known to cause a number of potentially life-threatening conditions in immunocompetent persons, including pneumonia, myocarditis, encephalitis, and the Guillain-Barré syndrome.<sup>3</sup> In patients with the acquired immunodeficiency syndrome, CMV infection may have additional manifestations, most notably retinitis and colitis. Although thrombocytopenia has been seen in patients with the acquired immunodeficiency syndrome who have CMV infections,<sup>4</sup> CMV-induced thrombocytopenia in immunocompetent adults appears to be rare, with only five previous cases having been reported (Table 1).<sup>5-9</sup>

Because CMV-induced thrombocytopenia has been reported so rarely in immunocompetent adults, it is difficult to know the natural course of this disease. In four of

the previously reported cases, symptomatic thrombocytopenia became evident within several weeks after the onset of infection.<sup>5-7,9</sup> In the fifth case, the time course was unclear because the patient had only serologic evidence of a previous CMV infection.<sup>8</sup> There were various responses to steroid treatment ranging from no response to normal platelet counts in two weeks. In addition, platelet counts often returned to normal as CMV titers declined, so it is difficult to know whether steroid therapy was of benefit. Splenectomy appeared to be useful in the two patients in whom idiopathic thrombocytopenic purpura was diagnosed,<sup>8,9</sup> but in the one patient in whom splenectomy was done specifically for CMV-induced thrombocytopenia,<sup>6</sup> there was no response.

The mechanism by which CMV induces thrombocytopenia is unknown, but two have been proposed: a direct cytopathic effect on megakaryocytes and an immune-mediated effect.<sup>9</sup> The distinction may have important therapeutic implications because an immune-mediated effect would be expected to respond to steroids but a cytopathic effect would not. In our patient, platelet counts were near normal for at least four weeks after the onset of infection, and symptomatic thrombocytopenia became evident only ten weeks after the onset. This temporal relationship suggests that an immune-mediated mechanism was responsible; a direct cytopathic effect of the virus would be expected to be evident much sooner in the clinical course.

The long latent period we observed also raises two clinical questions: Is asymptomatic thrombocytopenia a frequent occurrence after CMV infection? and are CMV infections responsible for some cases of thrombocytopenia that are misdiagnosed as idiopathic thrombocytopenic purpura? From the case we report, we conclude that for patients with acute CMV infection, a platelet count should be determined if there is evidence of petechiae, purpura, or bleeding, and for patients presenting with idiopathic thrombocytopenia, it may be worthwhile to examine for evidence of a previous CMV infection.

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